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CHANGES IN THE STATUS OF THE HUMAN TIBIA DURING ANTIORTHOSTATIC HYPOKINESIA

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16. Abstract

The purpose of this work was to study changes in biochemical properties of the human tibia during prolonged anti-orthostatic hypokinesia with different modes of motor activity and pharmacotherapy and comparison of results obtained with parallel examinations using ultrasonic diagnosis (UD) and photon absorptiometry (PA).

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CHANGES IN THE STATUS OF THE HUMAN TIBIA DURING ANTIORTHOSTATIC HYPOKINESIA

A. M. Tatarinov, A. I. Grigor'yev, V. V. Dzenis, Kh. A. Yanson, V. S. Oganov and A. S. Rakhmanov

The purposes of this work were study of changes in biomechanical properties of the human tibia during prolonged antiorthostatic hypokinesia with different modes of motor activity and pharmacotherapy and comparison of results obtained with parallel examinations using ultrasonic diagnosis (UD) and photon absorptiometry(PA). /134*

UD used the technique of surface sounding of the tibia on the medial surface using piezoelectrical exponential wave guides (PEW) with frequency 120 kHz [1 - 4]. Spot contact of the PEW with the studied surface makes it possible to measure on a fixed small base 10 mm and by detailed measurement of the bone obtain information not only about the average values of ultrasound velocity, but also about acoustic inhomogeneity of the bone. Measurements of velocity of ultrasound were made on ten bands of bone length; the height of each band was 1/10 of the total length of the bone from the edge of the proximal epiphysis to the base of the medial malleolus and was in limits from 3.3 to 4.3 cm in different subjects. The PEW were set on the anterior-medial surface of the crus with orientation of the measurement base parallel to the longitudinal axis of the bone in zones where thickness of the soft tissues was the least, but no less than 5 mm from the anterior edge of the tibia. Measurements were repeated three times in each band, and contact of the PEW with the crus tissues each time was re-established. Surface sounding by the PEW of the human tibia makes it possible to measure velocity of propagation of the bent wave of ultrasound in the compact bony tissue.

It was established that the greatest inhomogeneity in distribution of ultrasonic velocity over the length of the bone corresponds to increased degree of adaptation of the tibia to mechanical load; in this case the areas of maximum values of velocities were localized in the

*Numbers in margin indicate pagination in original foreign text.

middle of the diaphysis (at level of bands 4, 5), the areas of minimum values in the distal metaphysis (bands 8, 9), the greatest gradient of decrease in velocity on the distal section of the diaphysis (bands 6 - 8). In addition to change in the calcium content of the bone which can be traced from change in the average ultrasound velocities and PA readings, during hypokinesia one can expect loss of rheological adaptation of the bone to load whose mechanisms have not yet been studied, but as has been shown in [5, 6], the degree of rheological adaptation is reflected by the indicators of acoustic inhomogeneity. Variation in the shape of the ultrasound velocity distribution curve over the length of the bone governed by individual features and change in bone properties under different conditions of functioning is expressed as a difference in ultrasound velocity on the bands of the bone length, and displacement in the zones of maximum values over the length.

For UD the following indicators have been selected for distribution of ultrasound velocity (in the example of averaged curve of all participants in the experiment, Figure 1): average velocity for ten bands of bone $c_{10} = \sum_{i=1}^{10} c_i/10$ (i is the number of the band of bone length); /135

the standard deviation of average velocity for the bands of bone length $\sigma_c = \sqrt{\sum_{i=1}^{10} (c_{10} - c_i)^2/9}$ used in [4] as an individual indicator for bone inhomogeneity; difference in velocities in the proximal and distal metaphyses at levels of bands 2 and 9 $a_c = c_2 - c_9$, reflecting the magnitude and direction of change in velocity over the length; gradient of decrease in velocity on the distal section $\Delta_c = \Delta c^*/\Delta l^*$ (see Figure 1) suggested in [2] to evaluate the degree of adaptivity of the bone to the load. The indicator σ_c characterizes the total spread of velocity of bone, a_c and Δ_c are the specific features of its distribution curve over length.

The acoustic relief of the medial tibial surface to a great degree is inhomogeneous [5]; in making measurements by UD at 10 points on one line on the medial surface a certain leveling of the acoustic relief was permitted. Since repeated measurements with interval of a whole

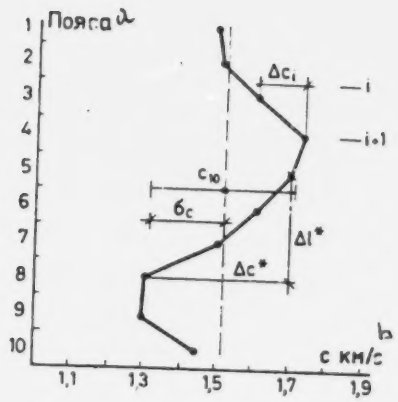

Figure 1. Determination of UD Indicators in Example of General Averaged Velocity Distribution Curve Over Length of Bone

Key:
a. bands
b. km/sec

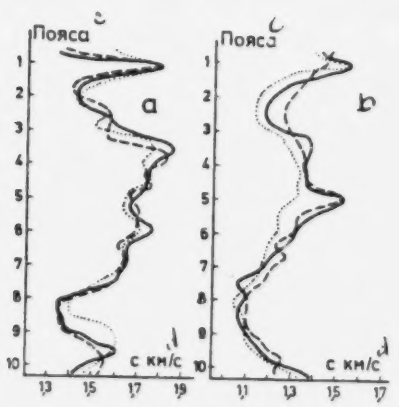

Figure 2. Examples of Acoustic Inhomogeneity of Medial Surface: Subject G (a) and K (b) (FT)

Key:

——— middle of medial surface
---- 0.5 cm closer to the front edge
.... 0.5 cm towards the interosseal edge
c. bands
d. km/sec

front did not preserve the markings of the sensor setting, it was important to reveal those bands which were located in the zones of the approximate acoustic plateau. The velocity changes in them with great reliability indicated differences in the properties of the bony tissue, and were not merely the result of its topographical inhomogeneity.

In order to establish these bands, the anterior-medial surface of the crus of all 15 participants in the experiment was measured once with background examination in more detail: the bone over the length was divided into 30 equal bands, measurements over the width were made on three lines in the middle of the medial surface, 5 mm closer to the front edge and 5 mm towards the interosseal edge. In this case the number of measurement points on the bone was 90. Examples of detailed ultrasonic measurement of the two sections of the experiment on the medial surface are presented in Figure 2. Its acoustic relief in different individuals varied, and the areas in relation to the plateau corresponded to different bands of bone length. Thus, for example in subject G (see Figure 2a) the points of greatest reliability for changes in properties of the bony tissue were at levels of bands 5 - 7. The average number of these points in the participants of the experiment was from 3 to 4. Consequently, in order to evaluate the properties of bony tissue in UD it is expedient to introduce yet another indicator, /136 the average velocity on bone bands where a relatively low gradient of velocity change exists along and transverse to the medial surface of the bone

$$c_{\text{п}} = \sum_{i=1}^{m} c_i/m;$$

here m is the number of these bands in the subject's bone.

The content of minerals in the contact tibial bone was determined by the PA method using the BMD (bone mineral detector) apparatus of the firm Gambro. Measurements were made on the crus with passage of a photon ray perpendicularly to the longitudinal axis of the bone at a level corresponding to bands 7, 8, the length of the bone with UD. Automatic conversion on a microcomputer made it possible to obtain data

regarding the content of minerals separately in the tibia and fibula, and to take into consideration the influence of changes in the cross-section of the bone over the course of the photon beam. Since the geometric dimension, the width of the photon beam, is a constant quantity, then the defined relative indicator for the content of mineral component (CMC) from the conditionally average cross-section area has dimensionality in grams per centimeter per square.

Studies using UD and PA were conducted within a 120-day experiment with antiorthostatic hypokinesia (angle of body inclination to the horizontal plane was -5°) based at the Institute of Medical and Biological Problems of the USSR Ministry of Public Health. Fifteen men of the third age group (19 - 44) according to the classification of the Institute of Gerontology of the USSR Academy of Medical Sciences were examined. Depending on prevention of the hypokinesia consequences, the experiment participants were distributed in four groups: control group (C), three people using pharmaceutical drugs (PD), four using physical training (PT), and group of complex prevention (PT+PD) four. PD were given to the experimental participants on the scheme suggested by A. I. Grigor'yev and B. V. Morukov. PT, the technique and cyclicity developed by A. V. Ovsyannikov and I. B. Kozlovskaya included exercises for muscles of the antigravitational band with monthly alternation of velocity, force, velocity-force modes and mode with passive stretching of the muscles. Parallel measurements using UD and PA were made during the background period, several days before the beginning of the hypokinesia, at the end of the first, second, third and fourth months of hypokinesia, during the period of restoration, on the fourth day after elevation and within one month. In order to exclude the influence of daily biorhythms on the ultrasound velocity of bone [3], studies on UD were made only in the morning.

Despite the fact that all the subjects belong to one age group and did not have any pathological deviation, the curves of ultrasound velocity distribution over the length of the bone differed strongly in them. This in the framework of each group of prevention determined the

spread of average velocities and velocities over the band of the bone. The greatest inhomogeneity in velocity was found in the bands of the distal part of the diaphysis which is characterized by a high gradient of its change over the length of the bone. Differences in ultrasound velocity distribution in bone and selection of the subjects without consideration for this circumstance meant that the averaged curves for the groups of prevention already during the background examination (Figure 3) differed fairly strongly. Moreover it is known that increased acoustic inhomogeneity of the bone of different individuals is natural for this age group [4].

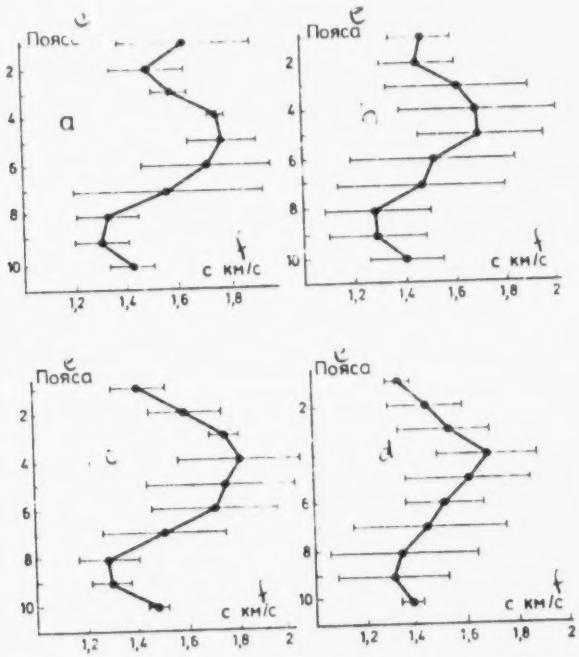

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Figure 3. Averaged Curves for Distribution of Velocity of Ultrasound Over Length of Bone and Standard Deviations on Bands for Groups C (a), PT (b), PD (c), PT+PD (d) with Background Examination

Key:
e. bands f. km/sec

The PA data for the background content of mineral component in /137 the bones of experiment participants also revealed inhomogeneity by

groups: C 1.64 ± 0.11 g/cm²; PT 1.70 ± 0.08 g/cm²; PD 1.68 ± 0.05 g/cm²; PT+PD 1.53 ± 0.07 g/cm². The averaged values for the content of mineral component by groups of prevention differed less than its values in people within the group; the greatest spread was noted in group C; the minimum value 1.49 g/cm², the maximum 1.85 g/cm². The results of examinations during observation demonstrated significant variability in the acoustic properties of the tibia from UD data and a certain change in the content of mineral component from PA data.

Changes in prevention groups. Because of the considerable spread of the UD and CMC indicators by groups and different trends of change in them in individuals from one group during the observation period for one average indicator of the prevention group it did not change statistically reliably. The diagrams for changes in the average UD and CMC indicators from PA data (Figure 4) could be used to evaluate the efficacy of the prevention method, while narrowing or expansion of the corridor for spread of indicators by groups on these diagrams could be used to evaluate the unequivocality of changes in individuals of one group.

In group C, a severe drop in average velocity c_{10} occurred within one month from the beginning of hypokinesia, then there was a trend towards restoration; the indicators σ_c and Δ_c during the entire period of hypokinesia dropped uniformly; a_c was maintained on the level of the background examination, although within one month of hypokinesia its value rose; CMC dropped continually during the first 3 months of hypokinesia, and in the fourth month there was a sharp increase exceeding the background level. In the PT group c_{10} decreased slightly by the second month of hypokinesia, then returned to the background; the indicators σ_c and Δ_c drop significantly during the entire period; a_c remained unchanged; CMC had a tendency to drop uniformly. In the PD group, none of the UD and PA indicators had a definite trend to change (on the average for the group), and as a result the values of the indicators by the end of hypokinesia differed little from the background. In the PT+PD group, velocity c_{10} dropping by the second month of /138

hypokinesia then returned to the background value; changes in σ_c and Δ_c were not regular; the value a_c increased noticeably; CMC had a tendency to a certain increase.

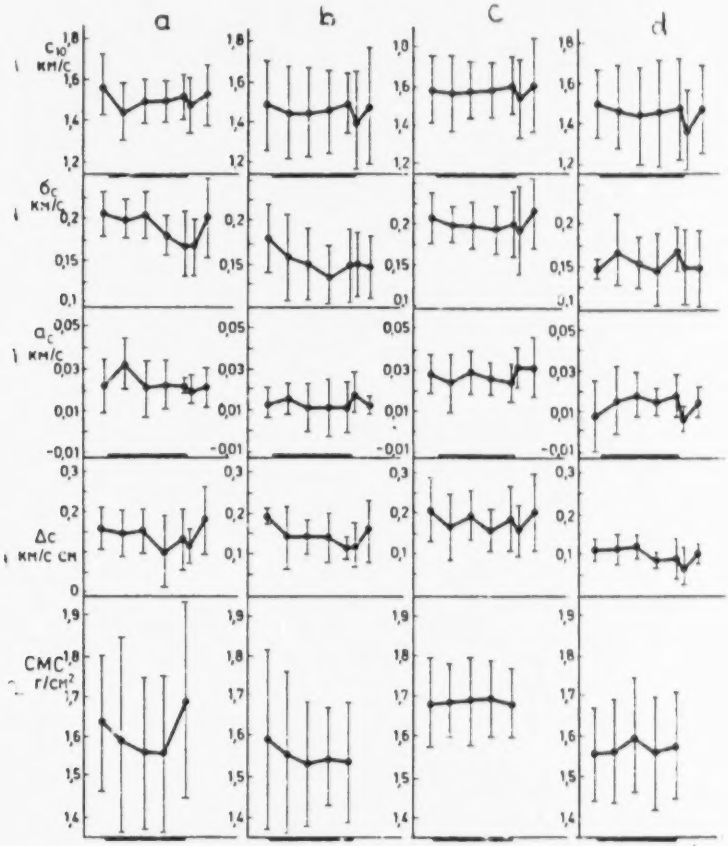

Figure 4. Diagrams for Changes in Indicators UD and PA in an Experiment for Prevention Groups: C (a), PT (b), PD (c), PT+PD (d).

The thick horizontal line designates the duration of the experiment.

Key:
1. km/sec
2. g/cm²

Changes in the corridor of standard deviations of the average UD and PA indicators by prevention groups in the majority of cases were not systematic. The corridor of spread c_{10} and CMC during 4 months of the experiment narrowed in the PT group, expanded in the PT+PD group.

Diagrams for change in c_n are not presented since the number and location in the bone of plateau points varied in the people, and standard deviation of c_n for the group was senseless.

In contrast to the average indicators for the prevention group, changes in the indicators c_n, a_c, Λ_c of UD in one participant of the experiment by months of bed rest as compared to the background could have a high degree of reliability. In order to evaluate reliability of the obtained change in ultrasound velocity, three values of velocity were used with repeated measurements at each point with the next examination period. It was established from the results of statistical analysis that at the points of the acoustic plateau, changes in velocity are statistically reliable with probability 95% with magnitude of absolute changes on the average exceeding 50 - 60 m/sec. During the experiment only 3 of the 15 subjects did not have unreliable changes /139 at the plateau points (one of the group C, two from PD). The maximum changes in velocity at the plateau points towards decrease were 340 m/sec, or 13.8% (subject from group PT+PD), 200 m/sec, or 15.4% (PT), 170 m/sec or 8.9% (PT), towards increase 290 m/sec or 16.6% (PT+PD), 170 m/sec or 14.8% (PD). The indicator Λ_c, the gradient for decrease in velocity on the distal section, has reliable differences with probability 95% with change in absolute values on the average for 10 m/cm x sec. Reliable changes towards decrease in Λ_c which have a stable nature (during 2 months and more) are noted in six cases (one in each of groups C and PD, two in PT and PT+PD); there were no such changes towards an increase.

TABLE. AVERAGE EFFECTIVENESS OF PREVENTION METHODS BY CHANGES IN INDICATORS UD AND PA FOR EXAMINED GROUPS

Place of Prevention Group by Efficacy	UD				PA; CMC
	c_{10}	c_n	σ_c	Λ_c	
I	PD	PD	PT+PD	PT+PD	PT+PD
II	PT+PD	TT+PD	PD	C	PD
III	PT	C	C	PD	C
IV	C	PT	PT	PT	PT

Evaluation of the efficacy of the prevention method was made by the sum of points accumulated in the prevention group from the data of changes in UD and PA indicators for each member of the group during the monthly examination. The criterion of prevention efficacy was maintenance of stability and increase in the indicators c_{10}, c_n, σ_c, Δ_c and CMC. The indicator a_c was not included among the criteria since it is still not clear how to interpret its changes. With a change in velocity c_{10} and c_n no higher than 30 m/sec, σ_c 10 m/sec, Δ_c 8 m/cm x sec, CMC 0.03 g/cm², the point equalled zero, in the interval up to the double value of deviation the indicator was 1, over the double value 2, deviations toward decrease had a negative sign, increase had a positive. The table presents the results of evaluating the prevention group: I place maximum sum of points, IV minimum. For the majority of indicators UD and PA, group PT and PD leads, in the second place PD, group PT occupies the last place. It is characteristic that determination of the efficacy of the prevention groups of hypokinesia by UD and PA methods mainly coincides.

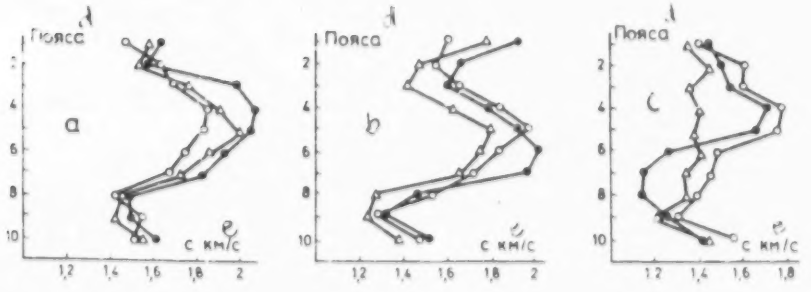

Figure 5. Changes in Velocity Over Length of Bone in Experiment

Key:

a. I group
b. II
c. III
●. background
Δ within 1 month
○ within 4 months
d. bands
e. km/sec

Changes by behavior groups. Analysis of individual changes in the UD and PA indicators in the participants of the observation made it possible to establish that changes in velocity c_{10} and c_n, as well as CMC during the observation correspond to one of three behavior schemes: decrease after one or two months to a minimum and return to the original value by the fourth month of the experiment (or tendency /140 to return, possibly also a certain exceeding of the background value): gradual increase and gradual decrease during the entire hypokinesia period. This made it possible to separate all the observation participants regardless of the prevention group into three groups of behavior: I group of "restoration", included six people; II "increase" five people; III "decrease" four people.

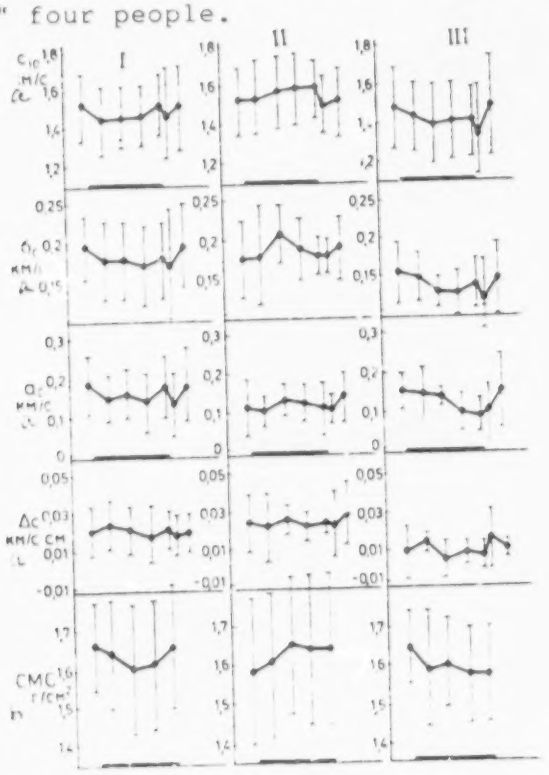

Figure 6. Diagrams for Changes in UD and PA Indicators by Behavior Groups

Key:
I. restoration
II. increase
III. decrease
a. km/sec
b. g/cm²

Figure 5 shows certain variants for change in the distribution curve of ultrasound velocity over the length of the bone as compared to the background within one month of hypokinesia and the end of the hypokinesia mode within 4 months. These examples could illustrate change in acoustic properties of the bone within three groups of behavior: I variant (a) the velocity of ultrasound could change on a definite section of the length of bone, most often in the diaphysis region (for example bands 3 - 6), and a certain smoothing of acoustic inhomogeneity occurred; II variant (b), the velocity decreased almost over the entire length of the bone within one month of hypokinesia and was restored by the end of observation; III variant (c) within one month of hypokinesia there was a sharp leveling of the curve over length because of significant decrease in velocity in the proximal region of the bone and increase in the distal; in this case the average velocity did not change. Further, velocity in the latter case began to rise in the proximal part which led to its overall increase.

Figure 6 presents the diagrams for changes in indicators UD and PA during hypokinesia for the group of behavior and spread of values of the indicators in the groups. As for the group of prevention, the spread for the group of behavior several times exceeds the average change in the indicator. Nevertheless, one can judge from the common nature of changes the interrelationship and the indicators of certain reaction of the bone to hypokinesia. For all behavior groups there was a correspondence between the directions of change in c_{10} and CMC which confirms the possibility of using UD to observe change in mineral composition of the bone. For I and II groups of behavior, the indicators of adaptation δ_c and Δ_c by the end of the experiment did not exceed the background value, and in group III significantly decreased. This indicates the independence of adaptation properties of the bone from the total content of mineral component. It is interesting that III group ("decrease") has significantly underestimated values of the indicator a_c determined by the difference in velocities of ultrasound from proximal and distal metaphysis. This feature is inherent to the prevention groups PT and PT+PD (see Figure 1) which include all four representatives of III group of behavior. Change in condition of the bone during /141

hypokinesia could be due not only to the prevention mode and its intensity, but to a less significant degree to individual features of the examined individuals.

In order to predict the probable behavior of the bony tissue during prolonged hypokinesia during background values of indicators UD and PA, a comparison was made of the average quantity c_{10}, σ_c, a_c, Δ_c and CMC and their variation by behavior groups from the data of the background period and the period of crisis. By crisis period we mean for group I the month of examination in which a decrease was found in velocity c_{10} up to the minimum value, the group II in the month of examination preceding the total increase in c_{10} or sharp jump, for group III the month of examination after the greatest decrease in c_{10}.

The average values of indicators c_{10}, σ_c and Δ_c and CMC differed for the behavior group, but the intervals of spread in the indicators were several times greater than the difference in the values of the indicators themselves during both the background and the crisis period. For indicator a_c we successfully revealed a law linking the magnitude of the indicator in relationship to average velocity a_c / c_{10} to the behavior of the bone during prolonged hypokinesia. The average values a_c/c_{10} for the behavior group significantly differ (Figure 7). The greatest values are group I, the least in group III, but the intervals of spread in all groups partially overlap. Sharp differentiation occurs during the crisis period, the average value a_c/c_{10} in groups I and II rises somewhat, and in group III drops slightly, while the interval of spread for group III is severely constricted, with a high degree of reliability distinguishes it from other groups, especially from I. Consequently, comparison of a_c/c_{10} for the relative magnitude of the total slope of the curve for change in velocity over length in individuals showing a decrease in ultrasound velocity and a tendency to decrease in CMC in the initial period of hypokinesia makes it possible to predict the further behavior of the bone, even greater decrease or restoration.

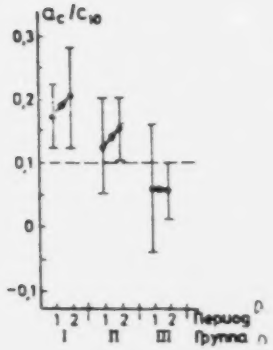

Figure 7. Distribution of Indicator a_c/c_{10} by Behavior Groups (I - III) During Background Period (1) and Crisis Period (2)

Key:
a. period b. group

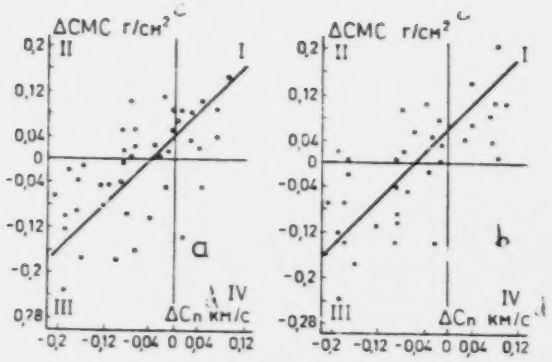

Figure 8. Correlation of Monthly Measurements as Compared to Background of Ultrasound Velocity Δ_{c_n} and ΔCMC in Bones of Observation Participants with Parallel Examinations (a) and With Displacement of ΔCMC by a Month Ahead as Compared to Δc_n (b)

Key:
c. g/cm^2 d. km/sec

It is apparent from the diagram for change in indicators UD and PA for prevention groups (see Figure 4) and behavior (see Figure 6) that the overall nature of change in c_{10} and CMC by groups often coincides. For a more detailed comparison of the results of the two techniques, correlation fields were constructed for change in velocity /142
c_n and CMC by points for each participant in the experiment. The velocity values c_n were selected from considerations of high reliability in the changes. No correlations were found between the absolute values of velocities and mineral density in the bones which is completely explained by the fact that the velocity of the bent wave of ultrasound depends not only on the rigidity of the bone material, which in turn is not determined unequivocally by the calcium content, but also on other parameters, for example, the thickness of the compact layer. During hypokinesia, even prolonged, the thickness of the compact layer does not change significantly, consequently, a link between Δc_n and ΔCMC is possible. Figure 8 presents correlation fields for change in Δc_n and ΔCMC as compared to background values obtained in monthly examinations of all experiment participants. In Figure 8-a the monthly deviations in Δc_n correspond to monthly ΔCMC defined by parallel measurements in the same month; in Figure 8-b the Δc_n values are placed in correspondence to ΔCMC defined a month later. As is apparent from Figure 8, the correlation fields are extended on the diagonal of the quadrants I - III, there is a large spread of points of relationship $\Delta c_n - \Delta$CMC . The linear correlation of the same monthly measurements Δc_n and ΔCMC looks like

$$\Delta CMC = 0{,}95\Delta c_n + 0{,}04 \ \text{g/cm}^2$$

(Δc_n km/sec; the coefficient of rank correlation r = 0.68); for the case of displacement of ΔCMC a month ahead

$$\Delta CMC = 0{,}96\Delta c_n + 0{,}06 \ \text{g/cm}^2$$

(r = 0.79). With shift of ΔCMC a month ahead as compared to determination of Δc_n, the correlation becomes close, experimental points emerge from the IV quadrant. The lack of points in IV quadrant indicatesthat

decrease in CMC in the bone could not result in increase in ultrasound velocity. At the same time, the presence of points in the II quadrant assumes the decrease in ultrasound velocity for reasons not related to washing of calcium from the bony tissue. The advance in the changes of UD as compared to the PA indicators (which proves an improvement in correlation with shift in ΔCMC) could be related to the fact that the PA readings depend on the total content of mineral substance in the bone both in the crystalline and in the amorphous state, while UD reacts to the change in elasticity of the osseous material, which could occur during transition of crystalline calcium into amorphous. Washing of calcium from the bone could not occur without its preliminary transition to the dissolved state, thus UD could be a forecasting technique indicating the possible leakage of calcium from the bone if the mode of the examined individual does not change.

No correlation was found between changes in UD indicators σ_c and Λ_c characterizing the adaptation qualities of the bone to the load, and changes in CMC during the experiment. At the same time a link is not excluded between laws of adaptation properties of the bone to the load with washing out of calcium, which could be indicated by decrease in σ_c, Λ_c and CMC in the PT prevention group (see Figure 4) and the III behavior group (see Figure 6).

Examinations during the restoration period were made using UD on the 4th day after elevation after 120 day hypokinesia and within a month after elevation. By the end of the restoration period all the averaged UD indicators for the prevention group were mainly returned to the background values. On the 4th day after elevation, the significant decrease in ultrasound velocities over the entire length of the bone was found in the overwhelming majority of experiment participants, which possibly is linked to fatigue processes resulting in decreased velocity of ultrasound in the bones of athletes during overloads [6].

Conclusions /143

1. During 120 day observation of the condition of the tibia in antiorthostatic hypokinesia and different modes of motor activity and

pharmacotherapy, a considerable variability was revealed in the acoustic properties of the bone (ultrasonic diagnosis) in the content of mineral component (photon absorbtiometry).

2. Average changes in prevention groups in the consequences of hypokinesia do not have statistical reliability because of the high initial spread of data and unequivocal changes in different individuals belonging to one prevention group.

3. Considerable statistically reliable changes were found in the acoustic indicators of the bone in different subjects by one of the possible behavior schemes: initial decrease with subsequent restoration, systematic increase or decrease and changes in mineral content corresponding to them.

4. The possibility was established of forecasting the probable decrease in mineral content of the bone using ultrasonic diagnosis.

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